

WHAT IS CLAIMED IS:

1. An oligonucleotide which is substantially complementary to a region of KSR RNA, wherein said oligonucleotide inhibits the expression of KSR.
2. The oligonucleotide of Claim 1 which is substantially complementary to a nucleic acid encoding mammalian KSR.
3. The oligonucleotide of Claim 1 which is substantially complementary to a nucleic acid encoding human KSR.
4. An oligonucleotide which is substantially complementary to a translation initiation site, 5' untranslated region, coding region or 3' untranslated region of mRNA encoding mammalian KSR.
5. An antisense oligonucleotide comprising a sequence substantially complementary to the CA1 region of KSR.
6. An antisense oligonucleotide comprising a sequence substantially complementary to nucleotides 124 to 243 (SEQ ID NO: 1) of the coding sequence of mouse KSR or nucleotides 97 to 216 of human KSR (SEQ ID NO: 25), or a portion thereof.
7. The oligonucleotide of Claim 6 comprising a sequence substantially complementary to nucleotides selected from the group of:
  - (a) 124 to 141 of the sequence of human KSR, corresponding to 151 to 168 of the sequence of mouse KSR (SEQ ID NO:3),
  - (b) 154 to 171 of the sequence of human KSR (SEQ ID NO:27)
  - (c) 181 to 198 of the sequence of mouse KSR (SEQ ID NO: 4); and

(d) 187 to 204 of the sequence of human KSR, corresponding to 214 to 231 of the sequence of mouse KSR (SEQ ID NO: 5).

8. An antisense oligonucleotide comprising a sequence selected from the group of SEQ ID NOS: 6-8 and SEQ ID NOS: 29-38.
9. The oligonucleotide of Claim 1 labeled with a detectable label.
10. The oligonucleotide of Claim 1 wherein the label is selected from enzymes, ligands, chemicals which fluoresce and radioactive elements.
11. The oligonucleotide of Claim 1 wherein said oligonucleotide comprises at least one phosphorothioate linkage.
12. A recombinant DNA molecule comprising a nucleic acid sequence which encodes on transcription an antisense RNA complementary to mammalian KSR RNA or a portion thereof.
13. The recombinant DNA molecule of Claim 12 wherein said nucleic acid sequence is operatively linked to a transcription control sequence.
14. A cell line transfected with the recombinant DNA molecule of Claim 13.
15. An expression vector capable of expressing a nucleic acid which is substantially complementary to the coding sequence of KSR RNA, or a portion/fragment thereof, wherein said oligonucleotide/nucleic acid inhibits the expression of KSR.

16. An expression vector capable of expressing an oligonucleotide which is substantially complementary to the CA1 region of the coding sequence of KSR RNA, or a portion/fragment thereof, wherein said oligonucleotide inhibits the expression of KSR.
17. A pharmaceutical composition comprising a therapeutically effective amount of an antisense oligonucleotide of claim 1 and a pharmaceutically acceptable carrier or diluent.
18. A composition comprising the oligonucleotide of claim 1 and a pharmaceutically acceptable carrier or diluent.
19. A composition comprising one or more chemotherapeutic or radiotherapeutic agent and an oligonucleotide which is targeted to a mRNA encoding mammalian KSR and which inhibits KSR expression.
20. A composition comprising an expression vector and a pharmaceutically acceptable carrier or diluent, wherein said expression vector is capable of expressing nucleic acid which is substantially complementary to the coding sequence of KSR RNA, or a portion/fragment thereof, wherein said nucleic acid inhibits the expression of KSR.
21. A method of inhibiting the expression of mammalian KSR comprising contacting cells which express KSR with an effective amount of a nucleic acid which is complementary to a portion of the mRNA encoding KSR.
22. A method of inhibiting the expression of mammalian KSR comprising contacting cells which express KSR with an effective amount of the oligonucleotide of Claim 1 whereby expression of mammalian KSR is inhibited.

23. A method of treating or preventing a hyperproliferative condition associated with the expression of gf-Ras or heightened expression of Ras in a mammal comprising administering to said mammal a therapeutically effective amount of a compound or agent which inhibits the expression of mammalian KSR protein.

24. The method of Claim 23 wherein said compound or agent is an antisense oligonucleotide which specifically hybridizes to a portion of the mRNA encoding KSR.

25. A method of treating or preventing a hyperproliferative condition associated with the expression of gf-Ras or heightened expression of Ras in a mammal comprising expressing in said mammal or administering to said mammal a therapeutically effective amount of a nucleic acid which is complementary to a portion of the mRNA encoding KSR.

26. A method of treating or inhibiting the progression of cancer in a mammal comprising administering to a mammal a therapeutically effective amount of a compound or agent which inhibits the expression of mammalian KSR protein.

27. The method of claim 26, wherein said cancer is selected from the group of pancreatic cancer, lung cancer, skin cancer, urinary tract cancer, bladder cancer, liver cancer, thyroid cancer, colon cancer, intestinal cancer, leukemia, lymphoma, neuroblastoma, head and neck cancer, breast cancer, ovarian cancer, stomach cancer, esophageal cancer and prostate cancer.

28. A method of treating or inhibiting the progression of cancer in a mammal comprising administering to a mammal a therapeutically effective amount of the oligonucleotide of Claim 1.

29. A method of conferring radiosensitivity to ionizing radiation in tumor cells in a mammal comprising administering to a mammal a therapeutically effective amount of a compound or agent which inhibits the expression of mammalian KSR protein.
30. A method of conferring radiosensitivity to ionizing radiation in tumor cells in a mammal comprising administering to a mammal a therapeutically effective amount of the oligonucleotide of Claim 1.
31. The method of Claim 29 or 30 wherein the tumor cells are cancer cells selected from the group of pancreatic cancer, lung cancer, skin cancer, urinary tract cancer, bladder cancer, liver cancer, thyroid cancer, colon cancer, intestinal cancer, leukemia, lymphoma, neuroblastoma, head and neck cancer, breast cancer, ovarian cancer, stomach cancer, esophageal cancer and prostate cancer.
32. A method of identifying compounds or agents which inhibit the expression of KSR comprising the steps of:
- (c) incubating a cell expressing KSR in the presence and absence of a candidate compound or agent; and
  - (d) detecting or measuring the expression of KSR in the presence and absence of a candidate compound or agent,
- whereby a decrease in the expression of KSR in the presence of said candidate compound or agent versus in the absence of said candidate compound or agent indicates that said compound or agent inhibits the expression of KSR.
33. A ribozyme that cleaves KSR mRNA.